Journal of Health Care and Research

Literature Review

DOI: https://doi.org/10.36502/2020/hcr.6165

Methamphetamine Induced Cardiomyopathy

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Received date: 05 May 2020; **Accepted date**: 21 May 2020; **Published date**: 02 June 2020

Citation: Younes I, Elkattawy S, Noori M, Posimreddy S. Methamphetamine Induced Cardiomyopathy. J Health Care and Research. 2020 Jun 2;1(2):78-82.

Abstract

Unfortunately, 35 million people worldwide suffer from drug use disorder while only one in seven people receive treatment. The health impacts combined with the socioeconomic burden of drug abuse are too numerous to count. It is well known that all organ systems are adversely affected by drug use including but not limited to the cardiovascular, respiratory, neurological, and renal. We will focus our attention on the effects of Methamphetamines on the cardiovascular system. Methamphetamines are known to be highly addictive stimulants with significant cardiovascular implications. We have gathered information from the literature available on methamphetamine-associated cardiomyopathy (MACM) and will discuss a case of a 58-year-old male, with no past medical history, who presented with dyspnea secondary to MACM.

Keywords

Methamphetamine, Cardiomyopathy, Pulmonary Artery Hypertension, Hypertension, Heart Failure

Introduction

The socioeconomic burdens of drug abuse are immeasurable. According to the United Nations World Drug Report of 2019, approximately 271,000,000 people between the ages of 15 and 64 years had used illicit drugs with a 30 % increase than it was in 2009 [1]. North America is the region with the highest prevalence of amphetamine and methamphetamine use [1]. Methamphetamine (MA) is a highly addictive central nervous system stimulant and associated with serious cardiovascular effects. Cardiovascular effects of methamphetamine include malignant hypertension, coronary artery disease, Coronary vasospasm, acute myocardial infarction, dysrhythmias, methamphetamine-associated cardiomyopathy (MACM), aortic dissection, and sudden cardiac death [2]. A study showed that cardiovascular disease was found to be the most common contributing cause of death among methamphetamine users [3]. However; early diagnosis of MACM can prevent further deterioration by guideline-based medical therapy and discontinuation of methamphetamine [4].

Case Presentation

This is a 58-year-old male, with no pertinent past medical history, who presented to the emergency department with dyspnea on exertion, orthopnea, and paroxysmal nocturnal dyspnea for the last 2 weeks. The patient denied any dyspnea at rest but reported dyspnea on minimal exertion. He reported weekly use of amphetamine for the last 10 years and >20 pack year smoking history; however, he denied any alcohol

use. Review of systems was negative for any recent chest pain, palpitations, productive cough, recent upper respiratory tract infection, fever, chills, or recent travel. His family history was insignificant for heart or lung diseases.

His vitals on admission were stable with a blood pressure of 130/93, heart rate of 108, respiratory rate of 18 and O2 saturation 98% on room air at rest. Physical exam was significant for an S3 gallop, jugular venous distention, bilateral lung crackles, and 1+ pitting edema. A chest x-ray showed moderately enlarged cardiac silhouette and mild bilateral pleural effusions.

EKG showed normal sinus rhythm with possible biatrial enlargement. Laboratory tests were significant for an elevated BNP>2500 with a normal ESR, CRP, EBV IgM/IgG, HSV Ab, TSH, and transferrin saturation. The aforementioned labs were sent to exclude other possible common causes of cardiomyopathy. A urine drug screen was positive for amphetamines. Transthoracic echocardiography was ordered based on clinical diagnosis of decompensated heart failure which revealed severely decreased left ventricular systolic function with an ejection fraction< 20 %with a mildly increased left ventricular cavity and severely dilated left atrium with RVSP 45.5 and TR Max Velocity 2.76 m/s (**Fig-1**). Left heart catheterization showed nonobstructive coronary artery disease with 50% stenosis proximal to mid LAD and ostial left circumflex artery (**Fig-2**).

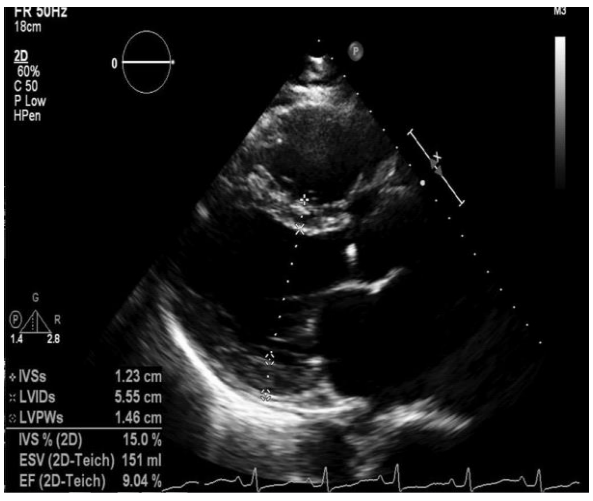

Fig-1: Echo

Severely decreased global left ventricular systolic function; elevated left atrial and left ventricular end-diastolic pressures.

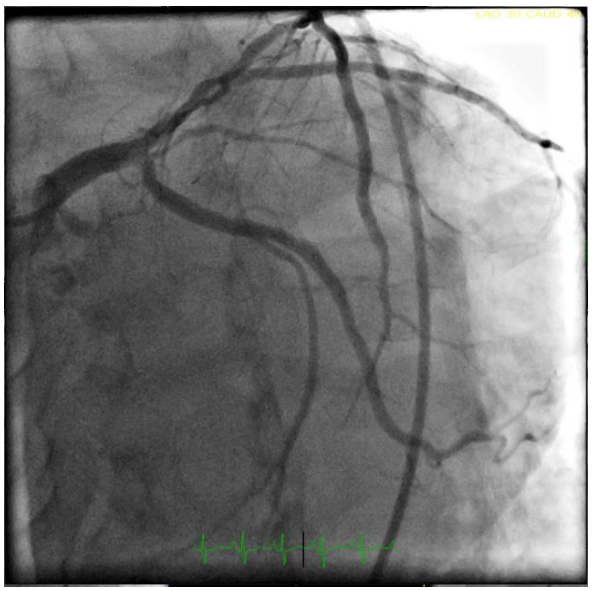

Fig-2: Left Heart Catheterization Report

This is a right dominant system. Left main coronary artery is normal. Proximal to mid segment of the LAD is heavily calcified. There is a diffuse 50% stenosis from the proximal to mid LAD. Diagonal vessels have no disease. Left circumflex coronary artery: Ostial left circumflex artery has 50% stenosis. OM branches have no disease. TIMI 2 flow.

Guideline-directed medical therapy for heart failure was started with furosemide, lisinopril, carvedilol, and aldactone. The patient continued to improve and was classified as New York Heart Association Class III on discharge and was scheduled for outpatient follow up in 1 month.

Discussion

Methamphetamines are highly addictive CNS stimulants that may be injected, smoked, inhaled, or ingested. They are sympathetic amines that act by elevating the levels of extracellular monoamine neurotransmitters (serotonin, dopamine, and norepinephrine) by promoting their release and blocking their reuptake at the nerve endings [5]. Elevated intrasynaptic monoamine levels affect multi organs encompassing neurological, psychiatric, and cardiovascular complications. The cardiovascular complications of methamphetamine vary from acute life-threatening complications such as malignant hypertension, coronary vasospasm, acute myocardial

infarction, aortic dissection, and sudden cardiac death to chronic complications such as methamphetamine-associated cardiomyopathy (MACM), pulmonary artery hypertension and right heart failure [2].

Methamphetamine induced hyperadrenergic state stimulates both peripheral alpha and beta adrenergic receptors resulting in hypertension [2]. Although it is recommended to start with alpha antagonist therapy and avoid B-adrenergic antagonist in the acute setting of pheochromocytoma, there are no evidence-based recommendations in the management of methamphetamine induced hypertension. In our case we used Carvedilol which is both an alpha as well as a beta antagonist.

MACM has been classified as dilated, hypertrophic and stress cardiomyopathy. Several case reports have described stress cardiomyopathy (Takotsubo or reverse-Takotsubo pattern) [6,7]. Our case showed dilated MACM with severely dilated left atrium and mild left ventricle dilatation with severely depressed systolic function. MACM has multifactorial and complex pathophysiology. Hyperadrenergic state, coronary vasospasm, ischemia, oxygen free radicals, and direct toxic effect are possible mechanisms of myocardial injury resulting in various pathohistological pictures of atrophy, hypertrophy, fibrosis, myolysis, cellular infiltration and edema [8,9]. A cohort study showed that dyspnea and angina pectoris are the most common symptoms in MACM. Our patient presented with dyspnea and denied any history of chest pain. The same study showed significant improvement of cardiac function and symptoms with discontinuation of methamphetamine abuse together with guideline-directed medical therapy compared to medical therapy only. This was suggested to be dependent on the degree of fibrosis and the irreversible myocytes damage [4]. The decision to implant devices (bi-ventricular pacing or ICD) into patients with MACM should be individualized and incorporate the medical therapy compliance, the likelihood of MA use relapse, and the probability of device infection especially in IV drug users [2].

Methamphetamine abuse is a common risk factor for aortic dissection after hypertension. Several cases have been reported in aortic dissection with MA use [10]. This association is probably secondary to the hypertensive effect. It was recommended to screen for methamphetamine abuse in young patients (less than 50 years old) presenting with aortic dissection [10]. Selective B-blockers as esmolol should be avoided in MA induced aortic dissection to evade the unpredictable effect of adrenergic alpha receptors stimulation. Alpha-antagonists, calcium channel blockers, nitrate, and B-blockers with alpha blocking activity can be used instead [10].

Angina is a common presenting symptom of MA abusers. MA most likely causes myocardial ischemia by similar mechanisms as cocaine which includes coronary vasospasm, thrombus formation, increased myocardial oxygen demand, and direct toxicity. It is unclear that MA is also atherogenic given increased catecholamine release resulting in an increase of blood pressure, platelet aggregation, and shear forces [11]. A pathologic study found that coronary artery disease is more common in MA abusers than controls, however; the former were older than the latter, lessening its reliability [12]. Case reports described MA induced myocardial infarction in the setting of normal coronary arteries, coronary artery stenosis, and significant coronary artery disease indicating different possible mechanisms of MA induced myocardial ischemia [11,13,14]. In our review, we also found three case reports describing myocardial infarction secondary to MA induced coronary artery dissection [15-17]. In patients with chest pain and EKG changes associated with troponin leak, coronary angiography or computed tomography of the coronary arteries should be considered.

Methamphetamine abuse is associated with a high incidence of pulmonary artery hypertension (PAH). This association was found to be in a certain subset of patients indicating genetic and environmental factors involvement. Few pathologic animal studies showed possible mechanisms for Methamphetamine induced PAH. One showed that the 5-HTT and 5-HT1B receptor expression was significantly increased in the MA group promoting pulmonary smooth muscle cell proliferation and remodeling of pulmonary arteries and this remodeling was found to be attenuated by fluoxetine

(SSRI) [18]. Another Study showed that methamphetamine may promote mitochondrial dysfunction and DNA damage by way of increased oxidative stress in pulmonary artery endothelial cells [19]. Orcholski and his colleagues used whole exome sequencing analysis and identified Carboxylesterase 1, a gene involved in drug metabolism, as a candidate gene for Meth-APAH [20]. Management of Meth-APAH begins with taking a good history and drug screening for patients diagnosed with PAH. Therapy for Meth-APAH is similar to the other form of PAH, however; it showed less response to inhaled nitric oxide challenge predicting less response to certain therapeutic agents as calcium channel blockers [21].

Conclusions

Non-obstructive coronary disease; endothelial dysfunction. Severely decreased left ventricular systolic function.

Conflict of Interest

All authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

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